DNDi launches drug development for pediatric AIDS

The Geneva-based not-for-profit organization, the Drugs for Neglected Diseases initiative (DNDi) has announced that they are to launch a drug-development program for the discovery of novel treatments for children with HIV/AIDS, adding the disease to sleeping sickness, leishmaniasis, Chagas disease and malaria, for which they already have drug-discovery programs for.

The WHO currently recommends antiretroviral treatment for all children with HIV under the age of two. However, current treatments do not have a child-adapted formulation or dose, and undesirable interactions with antitubercular drugs. Overcoming these factors is imperative for a successful pediatric HIV treatment and the DNDi, therefore, consulted with researchers and national organizations where the disease is endemic, such as South Africa and the Côte d’Ivoire, as well as those in the UK, France and the USA, in order to assess the desired specifications of new drugs. Following these discussions the DNDi has revealed that an improved first-line protease inhibitor will be their initial project.

Executive Director of the DNDi, Bernard Pécoul, stated in a press release that, ‘There are millions of children with HIV/AIDS in low- and middle-income countries, but their needs are absent from the HIV research and development agenda, and this is largely because they are poor and voiceless and do not represent a lucrative market. Working with partners, we hope to help fill this terrible gap and offer improved treatment options for children with HIV/AIDS.’

The program will be led by Marc Lallemant who was previously head of the Program for HIV Prevention and Treatment, a clinical research consortium of Chiang Mai University, Harvard School of Public Health, and Institut de Recherche pour le Développement, based in Thailand. In the press release Lallemant says that, ‘While we must make every effort to eliminate new HIV infections among infants through large-scale access to parental mother-to-child transmission and maternal antiretroviral therapy, we cannot neglect the millions of children currently and newly infected with the virus who are in dire need of treatment today.’


Austria–UK academic collaboration in TB research

The antitubercular activity of five synthetic evocarpine-related quinolones has been published by researchers from London- and Graz-based academic institutions. The collaboration studied the quinolones’ activity against the ATP-dependent MurE ligase of Mycobacterium tuberculosis as well as carrying out molecular docking studies on the compounds.

The teams utilized the spot culture growth inhibition assay in order to determine the minimum inhibitory concentration of each of the compounds against M. tuberculosis H37Rv, Mycobacterium bovis BCG and Mycobacterium smegmatis mc²155. Sanjib Bhakta (Birkbeck College, University of London, UK), who led the study, and his co-workers found the quinolones to have IC₅₀ values in the range of 95–207 μM when determined by HPLC and of 36–72 μM when analyzed by the phosphate detection colorimetric method for the inhibition of the MurE ligase of M. tuberculosis.

The docking element of the study was carried out using Glide and the M. tuberculosis MurE crystal structure. The findings showed that the uracil-recognition site of MurE was the probable binding site for the quinolones with GlideScores of -2.46 to -4.51 kcal/mol.

Bhakta and his colleagues believe that this initial study shows that the five quinolones studied have the potential to act as starting points for the development of increased-affinity MurE activity disruptors.